

ANOVA of ADHD score for the genotypes of 20 genes

Gene	Gene	11						12						22						F-ratio						p		Gene score														
		N			Mean SD			N			Mean SD			N			Mean SD																									
Dopamine genes																																										
<i>DRD1</i> SNP Ddel		Lit						Optimized						Lit						201																						
<i>DRD2</i> SNP Taq IA		Lit						Optimized						Lit						15						15.93		10.3														
<i>DRD3</i> SNP MscI		Lit						Optimized						Lit						152						17.68		11.2														
<i>DRD4</i> 4 bp repeat		Lit						Optimized						Lit						56						19.00		10.9														
<i>DRD5</i> 2 dinucleotide repeat		Lit						Optimized						Lit						74						18.63		11.4														
<i>DAT1</i> 3 repeat		Lit						Optimized						Lit						21						15.33		12.4														
Serotonin genes																																										
<i>HTT</i> 4 (<i>SLC6A4</i>) promoter ins/del		Lit						Optimized						Lit						85						16.20		10.9														
<i>HTR1A</i> SNP C-1918G		Ind						Optimized						Lit						82						19.00		10.61														
<i>HTR1B</i> (<i>HTR1D5</i>) SNP G861C		Lit						Optimized						Lit						202						18.49		10.9														
<i>HTR1DA</i> SNP T1350C		Ind						Optimized						Lit						266						18.16		11.3														
<i>HTR2A</i> SNP T102C MspI		Lit						Optimized						Lit						58						17.98		11.2														
<i>TDO2</i> SNP G->A Int 6fsf1		Optimized						Optimized						Lit						315						17.98		11.0														
<i>TPH</i> SNP A779 C		Lit						Optimized						Lit						60						19.00		10.4														

Figure 1 (a)
(continued)

Gene		11		12		22		F-ratio	p	Gene score
		N	Mean	SD	N	Mean	SD			
Norepinephrine genes										
<i>DBH</i> SNP Taq I	Lit									
	Optimized	67	18.81	10.1	168	18.78	11.1	101	16.69	11.3
<i>ADRA2A</i> SNP promoter region <i>MspI</i>	Ind									
	Optimized	186	17.42	11.1	128	18.8	10.5	22	21.95	11.7
<i>ADRA2B</i> delins	Ind									
	Optimized	155	18.14	11.5	158	18.46	10.6	23	19.73	9.6
<i>ADRA2C</i> 6 dinucleotide repeat	Ind									
	Optimized	131	18.77	10.5	113	15.79	11.0	92	20.17	11.2
<i>NET</i> (<i>SLC6A2</i>) SNP A1970G <i>Mnl</i>	Ind									
	Optimized	155	17.82	11.2	144	19.04	10.6	38	16.6	11.3
<i>PWNT</i> SNP G-148A	Ind									
	Optimized	110	16.89	11.1	156	19.59	10.9	66	17.58	10.9
<i>COMT</i> SNP val 158 met, G1947A, <i>NlaIII</i>	Ind									
	Optimized	75	19.42	10.8	175	18.52	11.0	86	16.52	10.8

Lit, references for literature-based gene scoring; Ind, gene scoring based on our studies of an independent set of subjects; SNP, single nucleotide polymorphism.
¹ *DRD4*: 11 = any < 4; 12 = 4/4; 22 = any > 4.
² *DRO4*: 11 = 148/148; 12 = het; 22 = non 148/non 148.
³ *DAT1*: 11 = non 10/non 10; 12 = 10/non 10; 22 = 10/10.
⁴ *HTR1A*: 11 = SS; 12 = SL; 22 = LL.
⁵ *HTR1A*, *TDC2* since there were only 2 22s, they were combined with the 12s.
⁶ *ADRA2C*: 11 = < 183/< 183; 12 = het; 22 = 183/183.

ANOVA of ADHD score for the Genotypes of Twenty Genes

Gene	11			12			22			F-ratio	p	Gene Score
	%	Mean	S.D.	%	Mean	S.D.	%	Mean	S.D.			

Other Neurotransmitter Genes

HTR6 SNP (Shinkai et al. 1998)

ADHD	2.8	12.33	9.7	27.1	18.26	10.3	70.0	18.66	11.2	1.44	.23	012	
ODD		3.0		2.3		3.91	3.1		3.64	3.2	.44	.64	021
CD		2.11		1.5		3.65	2.6		3.17	2.6	2.05	.13	022

GABRB3 dinucleotide repeat (Mutirangura et al. 1992)^a

ADHD	38.0	18.99	10.8	47.9	17.48	11.1	14.1	19.69	10.9	1.05	.35	102	
ODD		3.57		3.1		3.55	3.2		4.47	3.1	1.67	.18	002
CD		3.01		2.2		2.97	2.4		2.91	2.4	.089	.91	200

GABBR1 dinucleotide repeat (unpublished)^b

ADHD	9.5	17.5	11.7	27.0	19.1	11.7	63.5	18.2	10.5	.28	.752	020	
ODD		3.54		3.7		3.66	3.1		3.72	3.1	.047	.953	012
CD		3.45		2.6		2.72	2.2		3.02	2.4	1.24	.291	201

CNR1 (Cannabinoid 1 receptor) (Dawson 1995)^c

ADHD	10.6	19.35	10.9	44.7	18.25	11.0	44.7	18.13	10.9	.174	.83	200	
ODD		4.67		3.1		3.54	3.1		3.56	3.2	1.89	.15	200
CD		3.09		2.2		2.90	2.3		3.03	2.4	.146	.86	202

CHRNA4 (Cholinergic, nicotinic, alpha 4) (Weiland, Steinlein 1996)^d

ADHD	8.0	22.19	9.2	36.2	18.90	10.8	55.8	17.19	11.2	2.35	.096	210
ODD		5.07	3.0		3.59	3.0		3.55	3.2	2.74	.065	200
CD		3.11	2.1		2.93	2.3		2.99	2.4	.071	.930	200

NMDAR1 (Rupp et al. 1997) *Hpa* II SNP

ADHD	44.2	17.31	10.7	45.7	19.31	11.0	10.1	18.56	11.3	1.19	.303	021
ODD		3.79*	3.1		3.79*	3.1		4.84	3.1	2.93	.054	002
CD		2.83	2.3		3.07	2.3		3.28	2.7	.649	.523	012

ADORA2A (adenosine 2A receptor) (Deckert et al. 1996) C 108 T *Rsa* I.

ADHD	33.2	19.95	10.4	44.7	17.57	11.0	22.0	18.97	10.8	1.48	.229	201
ODD		4.04	3.3		3.41	3.1		4.02	3.1	1.52	.219	202
CD		3.39	2.5		2.82	2.1		2.83	2.4	2.04	.131	200

GRIN2B (glutamate ionotropic, NMDA 2B receptor) T/G (SNP database WIAF-1189).

ADHD	20.9	17.94	10.6	52.3	19.35	10.6	26.8	18.10	11.1	.582	.559	021
ODD		3.03*	3.0		4.15	3.1		3.50	3.1	3.22	.041	021
CD		2.36*	2.0		3.28	2.4		2.98	2.3	3.59	.029	021

NOS3 (nitric oxide synthase 3) (Wang et al. 1996)

ADHD	67.5	18.50	10.9	25.0	18.60	10.6	7.5	17.12	11.6	.186	.830	220
ODD		3.72	3.1		3.87	3.3		3.29	3.1	.311	.733	120
CD		3.00	2.3		3.12	2.2		2.33	1.9	1.08	.339	120

Opioids

PENK (proenkephalin) (Weber, May 1990; Comings et al. 1999a)^e

ADHD	32.1	18.71	10.4	47.4	18.02	11.3	20.6	18.25	11.0	.053	.948	201
ODD		3.75	3.2		3.75	3.2		3.48	3.1	.255	.775	220
CD		3.03	2.4		3.00	2.4		2.92	2.2	.041	.959	220

MME (enkephalinase) (see Methods)^f.

ADHD	33.9	19.44	11.0	50.9	17.34	10.9	15.2	19.53	10.9	1.26	.284	202
ODD		3.98		3.25		3.44		3.1		3.95		3.0
CD			3.10		2.4		2.81		2.3		3.32	

ANPEP (aminopeptidase N) (Watt, Willard 1990) and see Methods, A 257 G

ADHD	27.7	19.25	10.7	51.6	18.37	10.9	20.8	17.60	11.4	.398	.672	210
ODD		3.65		3.1		3.95		3.1		3.30		3.2
CD			3.12		2.4		3.05		2.4		2.42	

NAT1 (N-acetyl transferase) T 1088 A (Dietz et al. 1997; Comings et al. 2000)

ADHD	5.7	21.50	9.5	34.7	19.00	11.2	59.6	17.86	10.8	1.11	.329	210
ODD		4.94		3.7		3.51		3.2		3.68		3.1
CD			4.11		2.8		3.00		2.3		2.88	

Hormones and neuropeptides

ESR1 (estrogen 1 receptor) dinucleotide repeat (del Senno et al. 1992; Comings et al. 1999).

ADHD	27.3	19.08	12.0	41.2	17.52	10.6	31.5	18.90	10.3	.673	.511	201
ODD		3.82		3.4		3.56		3.0		3.86		3.0
CD			3.26		2.6		2.53*		2.0		3.33	

CYP19 (aromatase cytochrome P-450) dinucleotide repeat (Polymeropoulos et al. 1991b)^g

ADHD	13.4	16.88	11.6	45.2	17.28	11.7	41.4	19.76	9.9	2.11	.122	012
ODD		3.50		3.1		3.33		3.0		4.11		3.3
CD			3.07		2.4		2.52*		2.2		3.37	

SHBP (sex hormone binding protein) (Xu,Li 1998)

ADHD	59.8	18.39	11.2	35.2	18.38	10.4	5.0	17.44	11.4	.057	.944	220
ODD		3.61	3.1		3.76	3.1		3.50	3.1	.108	.897	120
CD		2.85	2.3		3.11	2.3		3.06	1.8	.465	.628	021

CRH (corticosteroid releasing hormone) (*Xmn I*, Genome Database)

ADHD	89.8	18.25	11.1	8.6	18.78	8.8	1.5	25.00	7.9	1.189	.285	012
ODD		3.66	3.2		3.71	2.8		5.60	3.2	.972	.380	012
CD		2.96	2.4		3.10	2.1		3.80	3.3	.370	.691	012

OXTTR (oxytocin receptor) (Liao et al. 1996) silent C->T in exon 3

ADHD	47.1	18.48	10.5	44.3	18.0	11.5		8.7	20.11	10.7	.431	.650	102
ODD		3.59	3.1		3.65	3.2		4.39	2.8	.776	.461	012	
CD		2.77	2.3		3.14	2.3		3.14	2.4	1.06	.347	022	

CCK C-45 T (Ishiguro et al. 1999)

ADHD	77.0	18.57	10.8	20.4	17.66	11.0	2.2	19.71	14.3	.227	.797	102
ODD		3.83	3.2		3.30	2.9		3.00	3.0	.909	.404	210
CD		3.04	2.4		2.71	2.2		3.14	2.3	.555	.574	102

INS (Hoban,Kelsey 1991; Gade-Andavolu et al. 1999)

ADHD	58.6	18.04	10.8	36.7	18.47	11.1	4.7	19.46	11.2	.147	.863	012
ODD		3.68	3.2		3.70	3.1		3.66	3.6	.0014	.998	120
CD		2.95	2.3		2.98	2.4		3.47	1.6	.334	.716	002

CD8 (Polymeropoulos et al. 1991a)^h

ADHD	23.2	17.5	11.3	44.3	18.54	10.9	32.5	18.42	10.9	.122	.885	021
ODD		3.31	3.2		4.09	3.2		3.44	3.0	1.95	.143	021
CD		2.53	2.1		3.27	2.5		2.92	2.1	2.44	.088	021

Figure 1(b)
 (Continued)

INFG (Wu,Comings 1998)

ADHD	21.8	18.22	10.9	58.3	18.17	10.9	27.9	18.82	10.8	.109	.896	102		
ODD		3.78		2.97		3.69	3.2			3.60	3.2	.068	.934	210
CD		3.11		2.4		3.01	2.4			2.82	2.0	.333	.717	210

PSI (Scott et al. 1996)

ADHD	36.0	17.78	11.1	48.0	18.56	10.6	15.2	18.19	11.6	.215	.806	021		
ODD		3.44		3.3		3.92	3.1			3.57	3.1	.828	.438	021
CD		2.59		2.1		3.18	2.4			3.30	2.5	2.68	.069	012

* Significantly lower than highest value by tukey test at $\alpha = .05$.

^a 11 = <188/<188, 12 = het. 22 ==188/=188

^b 11 ==10/=10, 12 = het. 22 =>10/>10

^c 11 = <5/<5 12 = het. 22 ==5/=5

^d 11 ==131/=131 12 = het. 22 =>131/>131

^e 11 ==178/=178 12 = het. 22 =>178/>178

^f 11 = a-c/a-c 12 = het. 22 = d-g/d-g

^g 11 = <4/<4 12 = het. 22 ==4/=4

^h 11 = 145/145 12 = 145/x 22 = x/x

Figure 1(b)
(Continued)

Final Results for the 42 Genes for the ADHD, ODD and CD traits

Trait	r	r ²	adjusted r ²	F	p	# genes
ADHD	.466	.217	.16	3.82	<.0001	22
ODD	.443	.196	.14	3.58	<.0001	20
CD	.451	.203	.15	3.94	<.0001	19

Figure 2

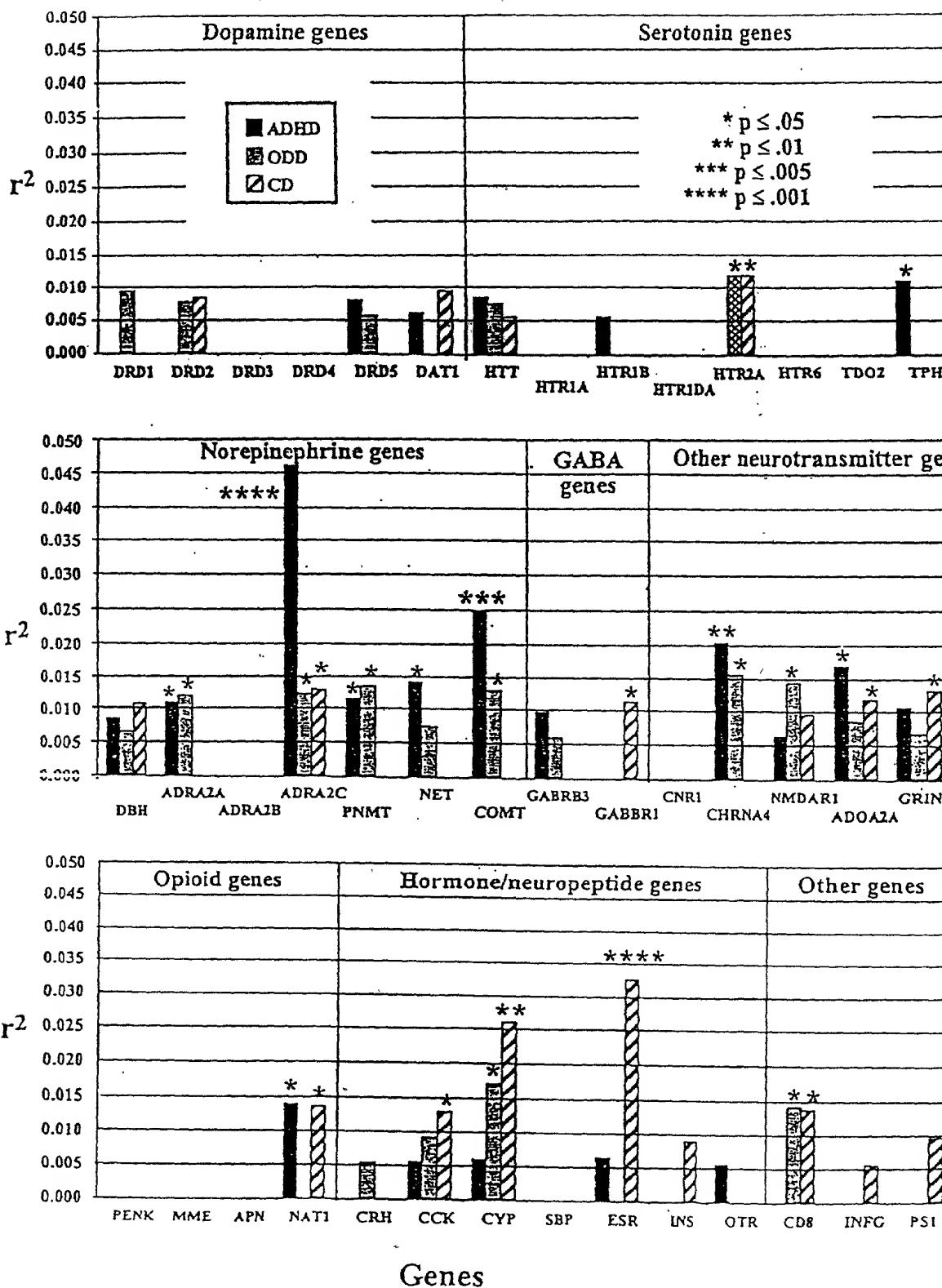


Figure 3

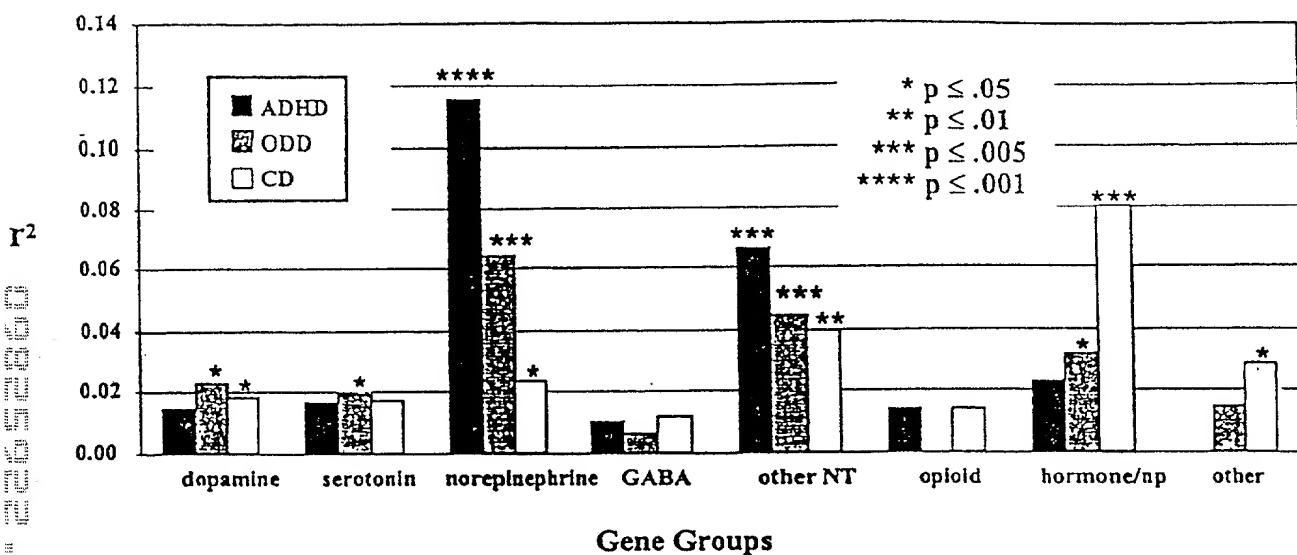


FIGURE 4